

# Hypertension

JOURNAL OF THE AMERICAN HEART ASSOCIATION



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## **Response to Treatment of Hyperuricemia in Essential Hypertension**

Philip B. Mellen, Anthony J. Bleyer and David M. Herrington

*Hypertension* 2007;49:46-; originally published online Apr 2, 2007;

DOI: 10.1161/HYPERTENSIONAHA.107.089938

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

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# Letter to the Editor

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## **Response to Treatment of Hyperuricemia in Essential Hypertension**

Epidemiologic evidence linking serum uric acid and incident hypertension is rapidly proliferating, and animal models of hyperuricemia have helped elucidate possible mechanisms for this relationship.<sup>1</sup> Furthermore, secondary analyses of clinical trial data suggest that the relationship between hypertension treatment and clinical outcomes is related to serum uric acid levels.<sup>2,3</sup> The logical next step is to evaluate whether targeting serum uric acid prevents hypertension or hypertension-associated end-organ damage. We agree with Trachtman<sup>4</sup> that well-designed, randomized, controlled trials should evaluate the efficacy of uric acid-lowering therapy in the prevention of hypertension.

We also note that the failure of allopurinol to prevent hypertension in spontaneously hypertensive rats does not necessarily contradict the hypothesis that uric acid plays a causal role in human hypertension. As the study by Trachtman et al<sup>5</sup> noted, serum uric acid levels do not differ between the spontaneously hypertensive rat and the normotensive Wistar-Kyoto strain. Like most mammals (and in contrast to humans), rats possess the hepatic enzyme uricase, which facilitates the rapid degradation of uric acid. Hyperuricemic rat models of hypertension have used oxonic acid to inhibit uricase, yielding modest elevations in serum uric acid more consistent with those seen in humans.<sup>1</sup>

Forthcoming studies will address whether uric acid is a viable target for the pharmacological prevention of hypertension in humans. If the results are positive, they will require a careful scrutiny of adverse outcomes, given the potentially broad application of this strategy for the prevention of hypertension.

## **Disclosures**

None.

**Philip B. Mellen**

*Department of Internal Medicine  
Section of General Medicine  
Wake Forest University Health Sciences  
Winston-Salem, NC*

**Anthony J. Bleyer**

*Department of Internal Medicine  
Section of Nephrology  
Wake Forest University Health Sciences  
Winston-Salem, NC*

**David M. Herrington**

*Department of Internal Medicine  
Section of Cardiology  
Wake Forest University Health Sciences  
Winston-Salem, NC*

1. Watanabe S, Kang DH, Feng L, Nakagawa T, Kanellis J, Lan H, Mazzali M, Johnson RJ. Uric acid, hominoid evolution, and the pathogenesis of salt-sensitivity. *Hypertension*. 2002;40:355–360.
2. Hoiegggen A, Alderman MH, Kjeldsen SE, Julius S, Devereux RB, de Faire U, Fyhrquist F, Ibsen H, Kristianson K, Lederballe-Pedersen O, Lindholm LH, Nieminen MS, Omvik P, Oparil S, Wedel H, Chen C, Dahlöf B. The impact of serum uric acid on cardiovascular outcomes in the LIFE study. *Kidney International*. 2004;65:1041–1049.
3. Franse LV, Pahor M, Di Bari M, Shorr RI, Wan JY, Somes GW, Applegate WB. Serum uric acid, diuretic treatment and risk of cardiovascular events in the Systolic Hypertension in the Elderly Program (SHEP). *J Hypertens*. 2000;18:1149–1154.
4. Trachtman H. Treatment of hyperuricemia in essential hypertension. *Hypertension*. 2007;49:e45.
5. Trachtman H, Valderrama E, Futterweit S. Nephrotoxicity of allopurinol is enhanced in experimental hypertension. *Hypertension*. 1991;17:194–202.